DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

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JUL 28 2005

Lachman Consultant Services, Inc.
Attention: Robert W. Pollock
1600 Stewart Avenue
Westbury, NY 11590

Docket No. 2004P-0405/CP1

Dear Mr. Pollock:

This is in response to your petition filed on September 8, 2004, requesting permission to file an Abbreviated New Drug Application (ANDA) for the following drug product: Tramadol Hydrochloride Oral Solution, 50 mg/mL. The listed drug product to which you refer in your petition is Ultram® (Tramadol Hydrochloride) Tablets, 50 mg, manufactured by Ortho-McNeil Pharm, Inc.

Your request involves a change in dosage form (i.e., from tablets to oral solution) from that of the listed drug product. The change that you request is the type of change that is authorized under Section 505(j)(2)(C) of the Act. However, for the reasons explained below, the Agency denies your request.

This petition was reviewed pursuant to Section 505(j)(2)(C) of the Federal Food, Drug, and Cosmetic Act (Act). Under Section 505(j)(2)(C)(i) of the Act such a petition will be approved unless the Agency finds that investigations must be conducted to show the safety and effectiveness of the proposed drug product, or of any of the active ingredients, the route of administration, the dosage form, or strength which differ from the listed drug product.

The Pediatric Research Equity Act (PREA) provides that a person who submits an application or supplement under Section 505 for a new active ingredient, new indication, new dosage form, new dosing regimen, or new route of administration shall submit assessments adequate to evaluate the safety and effectiveness of the drug or biological product for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration in each pediatric subpopulation in which the drug or biological product is safe and effective, unless FDA waives the requirement. 21 U.S.C. 355c(a). If a change proposed in a suitability petition triggers the need for pediatric clinical studies under PREA and FDA does not waive the requirement, the proposed product will not be eligible to be approved in an ANDA and the suitability petition must be denied.

Because you are seeking a change in dosage form, this proposed drug product triggers PREA. The listed drug to which you refer in your petition, Ultram, is not labeled for pediatric use. Accordingly, no Agency findings with respect to that approved product could be available to

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satisfy the PREA pediatric assessment requirements for your product. You would, therefore, be required to submit clinical pediatric studies.

Section 505B(a)(4)(A) (21 USC 355c(a)(4)(A)) provides for full waiver of the PREA pediatric assessment requirements if the Agency finds that: necessary studies are impossible or highly impracticable; there is evidence strongly suggesting the drug or biological product would be ineffective or unsafe in all pediatric age groups; or the drug or biological product does not represent a meaningful therapeutic benefit over existing therapies for pediatric populations and is not likely to be used in a substantial number of pediatric patients. You have offered no basis, and the Agency finds none, for concluding that any of these circumstances exist. Further, because it is an oral solution, FDA believes your product would provide a meaningful benefit over existing therapies and may be used in a substantial number of pediatric patients.

FDA, therefore, denies your petition because clinical trials are required under PREA for the approval of the requested change to the drug product and the Agency finds no basis for granting waiver of this requirement.[1]

In addition to the clinical trials required under PREA, we note that clinical trials are likely to be required to support the efficacy and safety of tramadol oral solution. Because the listed drug you seek to reference is approved for use in both acute and chronic settings, the rate of absorption of the drug is a critical parameter in determining whether the solution has the same pharmacodynamic properties as the tablet in terms of pain relief. It is unlikely that the pharmacokinetics of an oral solution will be the same as the tablet. Please contact the Division of Anesthetic, Critical Care and Addiction Drug Products at 301-827-7410 if you wish to pursue approval of your product under Section 505(b) of the Act.

If you disagree with our determination concerning the acceptability of your petition as originally submitted, you may seek a reconsideration of the denial following the procedures set forth in 21 CFR 10.33. Requests for reconsideration must be based solely on the information contained in your original petition and must be submitted in accordance with 21 CFR Section 10.20, in the format outlined in Section 10.33 and no later than 30 days after the date of the decision involved. Petitions for reconsideration should be filed with the Dockets Management Branch at the address

[1] We note your argument that because Ortho McNeil Pharmaceuticals received a written request under Section 505(A) to conduct pediatric studies for Ultram and received pediatric exclusivity for conducting the studies, your client should not be required to conduct studies on the same active moiety, Tramadol However, your application would be subject to Section 505B(a) ("New Drugs and Biological Products"), which requires any person who submits an application under Section 505 for certain types of changes, including a change in dosage form as in your case, to submit pediatric assessments of the drug. The grant of pediatric exclusivity to Ortho McNeil Pharmaceuticals is not relevant. As explained in the body of this letter, since Ultram is not fully labeled for pediatric use, the Agency findings with respect to that application could not satisfy your PREA requirement for pediatric assessment of the drug, and the Agency finds no basis for waiving this requirement with respect to your application.

listed below. If there is additional information, not included as part of your original submission that you would like the Agency to consider, you should submit a new petition including all the necessary information to the Dockets Management Branch.

A copy of this letter denying your petition will be placed on public display in the Dockets Management Branch, Room 1061, Mail Stop HFA-305, 5630 Fishers Lane, Rockville, MD 20852.

Sincerely yours,

Gary Buehler
Director
Office of Generic Drugs
Center for Drug Evaluation and Research